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Case Report

Dactylitis as a Manifestation of Sickle Cell Trait

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Abstract

Background/Introduction: Sickle Cell Disease is described by a wide range of signs and symptoms which usually result from the inherited abnormalities of hemoglobin, a compound found in red blood cells. These changes in turn modify the shape of the red blood cell to the characteristic sickled shape [1]. Both globin genes usually need to be abnormal, resulting in homozygous HbSS or heterozygous, such as β(beta-thalassemia (Hb S/β+-Thal or Hb S/β0-Thal) or hemoglobin C (HbSC) etc. for there to be any clinical manifestation and is usually called sickle cell disease [2]. Dactylitis is an acute swelling of the hands and/or feet in children and is often the earliest clinical sign of sickle cell disease [3].

Case Description: This case describes an 11-month-old female with known sickle cell trait presenting acutely with bilateral dactylitis of the hands. The patient was diagnosed clinically, and hemoglobin electrophoresis confirmed her trait status. The patient's symptoms resolved within 4 days.

Clinical Relevance: Dactylitis is thought by most clinicians to be exclusive to patients with either homozygous or multiple hemoglobin abnormalities and is usually not considered in heterozygous patients with clinical evidence of a normal allele [4]. Current literature includes few references with regards to this presentation in sickle cell trait patients [5]. A broader context of the manifestation of sickle cell trait can assist physicians with improved diagnosis and long-term patient management.

Keywords: *Sickle-Cell Trait; Dactylitis; Electrophoresis*

Abbreviations

ED: Emergency Department; HbA: Hemoglobin A; HbA2: Hemoglobin A2; HbS: Hemoglobin S; HbSC: Hemoglobin SC; HbSS: Sickle Cell Hemoglobin; MCV: Mean Corpuscular Volume; RDW: Red Cell Distribution Weight; Thal: Thalassemia; WBC: White Blood Cell

Introduction

Dactylitis, also known as hand-foot syndrome, is an acute vaso-occlusive complication characterized by pain and edema in both hands and feet and is frequently associated with an increase in local temperature and erythema [6]. With respect to sickle cell disease, it is most often seen in patients with homozygous Hemoglobin S or Hemoglobin SC heterozygotes [2]. The edema observed is typically non-pitting and generally more prominent in the fingers, toes, or dorsum of hands or feet [4].

The pathophysiological foundation for dactylitis is due to localized infarction arising from the sickling of red blood cells in the bone marrow. This in turn causes stasis of blood and sequestration of cells. The natural consequences are ischemia and tissue hypoxia which worsen the sickling process [7]. Often times these infarctions occur in the diaphysis of the small tubular bones of the hands and feet in young children which causes tissue necrosis at the metacarpals, metatarsals, and phalanges resulting in dactylitis [4,5,7].

In our case, the patient presented with bilateral dactylitis of the hands which is unusual due to her heterozygous state with a normal hemoglobin allele. It is pertinent to evaluate this patient due to the clinical relevance of such findings in preventing further possible complications by adjusting the management of what is generally thought to be a predominantly benign condition.

Case Report

The patient is an 11-month-old female with sickle cell trait diagnosed via state newborn screening who presented to the pediatric Emergency Department during a winter month with one hour of bilateral finger swelling. Her mother reported that she was getting the patient ready for bed when she noticed her fingers were swollen so she immediately brought her in to be evaluated as this was the first occurrence. She denied any fevers, recent illness in the child and recent travel. She reported the child had no changes in oral intake or urine output and was at her baseline state. The only sick contact was the patient's brother who had 1 day of gastroenteritis. When questioned about possible inciting factors mother noted that the patient had been removing her mittens frequently whenever she goes outdoors in cold weather. Her birth history was unremarkable; the patient was born full term via repeat Caesarian section, birth weight of 8 pounds, no complications in pregnancy and no NICU stay. The patient was not on any medications, had no surgeries or hospitalizations and no allergies. Immunizations were up to date except for the influenza vaccines. Her family history was significant in that her father has sickle cell -beta thalassemia and her brother has beta thalassemia trait according to her mother. Developmentally, the patient was appropriate for age and meeting all milestones.

On arrival to the emergency department, the patient's vitals showed a temperature of 97.5F rectally (in our hospital all children under age 3 get a rectal temperature during triage by the nurses), heart rate of 120, respiratory rate of 22 and oxygen saturation of 98 percent. Physical examination showed an active female infant in no acute distress. All fingers of both hands were swollen, sausage shaped and erythematous at the bases. There were no obvious signs of trauma, bruising or any insect bite marks noted on both hands. On gentle palpation, fingers were warm with non-pitting edema noted on the dorsum of both hands. The range of motion of all extremities were intact. When the hands were touched the patient would pull her hands away possibly indicating mild pain. No further swelling was noted on any other joint.

The patient's recent CBC showed WBC: 6.2, hemoglobin 11.3, hematocrit: 37 MCV 63 and RDW 14.9. She was given Motrin and hot compress was applied for pain and to reduce any swelling. As patient was comfortable, not in any acute distress, afebrile and moving both hands, no X-ray was performed to avoid exposing the child to unnecessary radiation at the time. The patient was referred to pediatric hematology clinic to be seen later that day. She returned to the hematology clinic within 12 hours since the beginning of symptoms with an identical physical examination and no reduction in swelling. Patient was still afebrile and not in any acute distress. The patient was evaluated by the pediatric hematologist who confirmed the clinical diagnosis of dactylitis and hemoglobin electrophoresis was ordered. Mother was advised to continue giving child Motrin 10 mg/kg at home along with warm compresses at regular intervals to alleviate the swelling. She was advised to contact the hematologist or return to the emergency room if any changes developed. Hemoglobin electrophoresis resulted in HgA 67.0% Hg A2 2.6% and HgS 30.4% with reflex Sickle Cell Prep positive for sickling. Mother was contacted and noted that the swelling resolved in 4 days with the use of warm compresses and the patient remained in no distress throughout with no changes in appetite or behavior. Mother counseled on the expectations of having a child with sickle cell trait and a follow up appointment for 6 months was scheduled.

To date, there is only one case report relating dactylitis in a patient with sickle cell trait. In comparison to our case the findings of dactylitis in the previously reported case involved both hand and feet and occurred in the hospital setting while the patient was being treated for fever, gastroenteritis and dehydration. In the previous case, the hand swelling of the patient resolved in 4 days and the feet resolved in 7 days [5].

Discussion

The sickle cell is one of the most common hemoglobinopathies present in humans. In malaria-endemic regions, mutations in the B-globin gene producing sickled hemoglobin often conferred a distinct survival advantage [1]. This is demonstrated by the prevalence of the sickle cell trait being as high as 25% - 30% in western Africa with approximately 120 000 annual births with sickle cell disease [8] compared to 8% to 10% percent among African Americans with 4000-5000 annual sickle cell disease births [9]. The vaso-occlusion characteristic of sickle cell disease often manifests itself in several ways such as chronic hemolytic anemia, recurrent painful episodes, and chronic organ damage [1]. Dactylitis, or hand-foot syndrome is one of these manifestations.

Dactylitis is most common between the age of 6 months and 2 years in patient who have sickle cell disease with the highest prevalence between the ages of 6 to 12 months of age [4,10-12]. Quite often it is the earliest presenting manifestation of sickle cell anemia in approximately 30% of cases and in one study of children with homozygous HgSS, 24 percent of patients experienced dactylitis before 12 months [3,4]. Various estimates of the prevalence of dactylitis in childhood have been reported; from 11% in the United States, to 45% in Jamaica, and as high as 80% in Africa [10,12].

In infants with the disease, anemia usually begins at around age 6 months due to the replacement of normal fetal hemoglobin (hemoglobin F) by abnormal hemoglobin S. Classically, children with sickle cell disease manifest the acute swelling of the dorsum of the hands and/or feet beginning around age of 6 months and is accompanied by fever, leukocytosis and mild anemia [13,14]. Symptoms last on average 14 days [6,13] and it is precipitated most frequently during the colder months [4,15,16]. Incidence of dactylitis decreases by age of 7 years of age due to the regression of red bone marrow subsequent fibrosis with increasing age [3,17,18]. Recurrence of dactylitis is not uncommon and was previously found to be present in 41% of cases [4]. The diagnosis of dactylitis is generally made by history and physical examination [19]. Roentographically there is initially limited changes seen besides evidence of soft tissue swelling but in 2 - 3 weeks subperiosteal new bone appears with cortical thinning and intramedullary densities seen in the affected bones [13,16].

Regarding the differentials of dactylitis, osteomyelitis, reactive arthritis and juvenile idiopathic arthritis must also be considered [5,6]. Our patient was afebrile, showed no leukocytosis and her symptoms resolved in four days without the use of antibiotics. Furthermore, she had no recent illnesses or rashes, received no vaccinations within the past 5 months, showed no urethral or conjunctival symptoms, her swelling was constant without improvement throughout the day and there was no involvement of the lower extremities or large joints, all of which are uncharacteristic arthritis traits [20,21].

Sickle cell trait is generally perceived by most clinicians as a benign condition under basal conditions due to the protective effect of the normal hemoglobin allele. The usual partition of Hb A and Hb S in sickle cell trait on hemoglobin electrophoresis is approximately 60: 40 owing to a greater posttranslational affinity of α chains for β A than for β S chain [22].

However, there are a few key clinical sequelae of the sickle cell trait, such as; hematuria and hyposthenuria [23] splenic infarction (especially at high altitude) [24] and an increased risk for venous thrombosis [25]. The trait is also associated with renal medullary carcinoma [26] and an a substantially increased, age-dependent risk of exercise-related sudden death amongst armed forces recruits in basic training [27].

This is of key importance as the onset of dactylitis has been studied as a key predictor of adverse outcome and the severity of sickle cell disease [28,29]. In one study, there was noted to be a relative risk of severe disease estimated at 2.67 compared to persons with when dactylitis occurred before the age of 1 year was previously noted [28].

In our case, it is rather unusual to note the clinical presentation of dactylitis in a known sickle cell trait patient with the expected levels of Hemoglobin S confirmed via hemoglobin electrophoresis. This raises the question of there possibly being other hemoglobin variants present in our patient [30,31]. Due to the scarcity of clinical reports on such cases, there is no present evidence regarding the future course of the heterozygous state with homozygous presentation.

Conclusion

A confirmed sickle cell trait patient presenting with dactylitis is an unusual clinical occurrence and highlights the sometimes-false sense of security regarding heterozygotes. However, it draws attention for increased investigation into the varying manifestations of sickle cell trait and thereby decrease prevailing misconceptions of the trait as a benign or symptomless condition. A high clinical suspicion for underlying causes and possible future complications coupled with increased vigilance will allow providers to modify their management of such patients while being able to provide appropriate counselling of patients.

Bibliography

1. Hoffman Ronald., *et al*. "Hematology: Basic Principles and Practice". Seventh edition, Elsevier (2018).
2. Kupersmith Lee M., *et al*. "Sickle Cell Anemia and the Hand". *Journal of the American Society for Surgery of the Hand* 3.3 (2003): 145-151.
3. Babhulkar SS., *et al*. "The Hand-Foot Syndrome in Sickle-Cell Haemoglobinopathy". *Journal of Bone Joint Surgery* 77B.2 (1995): 310-312.
4. MCG Stevens., *et al*. "Observations on the Natural History of Dactylitis in Homozygous Sickle Cell Disease". *Clinical Pediatrics* 20.5 (1981): 311-317.
5. Jadavji T and Prober CG. "Dactylitis in a Child with Sickle Cell Trait". *Canadian Medical Association Journal* 132.7 (1985): 814-815.
6. Da Silva Junior GB., *et al*. "Osteoarticular Involvement in Sickle Cell Disease". *Revista Brasileira De Hematologia E Hemoterapia* 34.2 (2012): 156-164.
7. Ejindu VC., *et al*. "Musculoskeletal Manifestations of Sickle Cell Disease". *Radiographics* 27.4 (2007): 1005-1021.
8. Fleming AF. "The Presentation, Management and Prevention of Crisis in Sickle Cell Disease in Africa". *Blood Reviews* 3.1 (1989): 18-28.
9. Motulsky AG. "Frequency of Sickling Disorders in U.s. Blacks". *The New England Journal of Medicine* 288.1 (1973): 31-33.
10. Trowell HC., *et al*. "The Natural History of Homozygous Sickle-Cell Anaemia in Central Africa". *The Quarterly Journal of Medicine* 26.104 (1957): 401-422.
11. Diggs LW. "Bone and joint lesions in sickle-cell disease". *Clinical Orthopedics* 52 (1967): 119-143.
12. Lambotte-Legrand C. "Hand-Foot Syndrome in Sickle-Cell Disease". *JAMA: The Journal of the American Medical Association* 104.2 (1963): 200-201.
13. Worrall VT and Butera V. "Sickle-Cell Dactylitis". *The Journal of Bone and Joint Surgery. American Volume* 58.8 (1976): 1161-1163.
14. Salma AlDallal. "Dactylitis: A Complication in Patients With Sickle Cell Disease". *American Research Journal of Hematology* 1.1: 27-31.
15. Amjad H., *et al*. "Letter: Sickling Pain and Season". *British Medical Journal* 2.5909 (1974): 54.
16. Redwood AM., *et al*. "Climate and Painful Crisis of Sickle-Cell Disease in Jamaica". *British Medical Journal* 1.6001 (1976): 66-68.
17. Watson RJ., *et al*. "The Hand foot Syndrome in Sickle-Cell Disease in Young Children". *Pediatrics* 31.6 (1963): 975-982.
18. Samir K Ballas., *et al*. "Beyond the Definitions of the Phenotypic Complications of Sickle Cell Disease: An Update on Management". *The Scientific World Journal* (2012): 949535.

19. Vichinsky E. "Overview of the clinical manifestations of sickle cell disease". In: UpToDate, Schrier SL (Ed), Waltham, MA (2019).

20. Plesca DA, *et al*. "Postinfectious Arthritis in Pediatric Practice". *Maedica* 8.2 (2013): 164-169.

21. Weiss PF. "Oligoarticular juvenile idiopathic arthritis". In: UpToDate, Klein-Gitelman M (Ed), UpToDate, Waltham, MA (2019).

22. Lorey F., *et al*. "Universal Screening for Hemoglobinopathies Using High-Performance Liquid Chromatography: Clinical Results of 2.2 Million Screens". *European Journal of Human Genetics* 2.4 (1994): 262-271.

23. Diggs LW. "The Sickle Cell Trait in Relation to the Training and Assignment of Duties in the Armed Forces: Iii. Hyposthenuria, Hematuria, Sudden Death, Rhabdomyolysis, and Acute Tubular Necrosis". *Aviation, Space, and Environmental Medicine* 55.5 (1984): 358-364.

24. Lane PA. "Splenic Syndrome at Mountain Altitudes in Sickle Cell Trait. Its Occurrence in Nonblack Persons". *JAMA: The Journal of the American Medical Association* 253.15 (1985): 2251-2254.

25. Tsaras G., *et al*. "Complications Associated with Sickle Cell Trait: A Brief Narrative Review". *The American Journal of Medicine* 122.6 (2009): 507-512.

26. Davis Charles J., *et al*. "Renal Medullary Carcinoma the Seventh Sickle Cell Nephropathy". *The American Journal of Surgical Pathology* 19.1 (1995): 1-11.

27. Colman N. "Interaction of Alpha-Thalassemia and Homozygous Sickle-Cell Disease". *The New England Journal of Medicine* 306.24 (1982): 1441-1446.

28. Foucan Lydia., *et al*. "Early Onset Dactylitis Associated with the Occurrence of Severe Events in Children with Sickle Cell Anaemia. the Paediatric Cohort of Guadeloupe (1984-99)". *Paediatric and Perinatal Epidemiology* 20.1 (2006): 59-66.

29. Miller ST., *et al*. "Prediction of Adverse Outcomes in Children with Sickle Cell Disease". *The New England Journal of Medicine* 342.2 (2000): 83-89.

30. Monplaisir Nicole., *et al*. "Hemoglobin S Antilles: A Variant with Lower Solubility Than Hemoglobin S and Producing Sickle Cell Disease in Heterozygotes". *Proceedings of the National Academy of Sciences of the United States of America* 83.24 (1986): 9363-9367.

31. Witkowska HE., *et al*. "Sickle Cell Disease in a Patient with Sickle Cell Trait and Compound Heterozygosity for Hemoglobin S and Hemoglobin Quebec-Chori". *The New England Journal of Medicine* 325.16 (1991): 1150-1154.

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